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Gregg B. Morin  
Name

April 11, 2005  
Date

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Inventors: Thomas R. Cech et al.

Filing Date: January 11, 2002

Serial No: 10/044,539

Docket: 015389-002630US; 018/212c

Title: MAMMALIAN CELLS THAT HAVE  
INCREASED PROLIFERATIVE CAPACITY

Art Unit: 1632

Examiner: Louis D. Lieto, Ph.D.

**DECLARATION UNDER 37 CFR § 1.132**

**BY GREGG B. MORIN, Ph.D.**

Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

I, GREGG B. MORIN, do hereby declare as follows:

1. I am a co-inventor on the above-referenced patent application, and am familiar with its contents. I have been a research scientist in the field of molecular biology for about twenty years, and am currently Head of Proteomics at the Michael Smith Genome Sciences Centre in Vancouver, British Columbia.

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2. The claims currently under examination at the Patent Office cover mammalian cells containing a recombinant polynucleotide encoding human telomerase reverse transcriptase (hTERT).  
I understand the Patent Office has raised the question of whether someone reading the disclosure at the time it was filed would have known how to make fragments of the hTERT protein encoded by SEQ. ID NO:1 that would still have telomerase catalytic activity when associated with telomerase RNA component.
3. It is standard procedure in determining the structure-function relationship of any protein to truncate the sequence from either terminus until there is loss in function. The minimal fragment that retains function defines the core sequence needed for activity.
4. I enclose two scientific papers describing the use of terminal deletion analysis to map functional domains within a protein sequence. The first paper by Cherry et al. (Plant Cell 5:563-575, 1993) maps the functional regions of oat Phytochrome A. The second paper by Kawakami et al. (Nucleic Acids Res. 24:303-310, 1996) maps the functional regions of mouse homeobox protein ARRC3. These papers were published some time before the filing of our first hTERT patent application, showing that fragmentation analysis was a well-known and often used strategy of protein analysis.
5. In a similar fashion, the core sequence of hTERT could be determined by fragmentation analysis in combination with functional testing. Once the core sequence is identified, fragments of hTERT smaller than the entire full-length protein but containing the core sequence would be expected to retain function. Smaller versions of the native protein that retain activity may be more easy to crystallize. They may be better for use in vitro, in vivo, or for biomedical applications because other activities or functions normally mediated by the deleted part of the sequence have been eliminated.

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6. One way active hTERT fragments could be found would be to start with an expression plasmid like pGRN121, described in Example 6 (SEQ. ID NO:1 in the EcoRI site of pBluescriptII SK+). One or more codons can be removed by recombinant techniques from either end of the hTERT encoding sequence, thus creating a vector for expressing the truncated protein. The vector could then be expressed in a reticulocyte lysate system along with hTR (telomerase RNA component) and assayed for telomerase activity using the same methodology shown in Example 7.
7. In my expert opinion, someone skilled in recombinant DNA technology as it was in 1997 and guided by the information in this patent application would have been able to perform this type of fragmentation study as a matter of routine experimentation.
8. I hereby declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

7 April 2004  
Date

  
Gregg B. Morin, Ph.D.  
Vancouver, B.C., Canada